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Macroscopic hematuria in mesangial IgA nephropathy: Correlation with glomerular crescents and renal dysfunction

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Macroscopic hematuria in mesangial IgA nephropathy: Correlation with glomerular crescents and renal dysfunction. One hundred and eighty-six renal biopsy specimens from 79 adult patients with mesangial IgA nephropathy were examined and correlated with clinical data at the time of biopsy. Forty patients (group 1) with a history of macroscopic hematuria were compared with 39 patients (group 2) without such a history. Group 1 patients had a higher serum creatinine, 240 ± 20 μmoles/liter vs. 140 ± 10 μmoles/liter ($P < 0.01$), lower creatinine clearance 69 ± 36 ml/min vs. 87 ± 30 ml/min ($P < 0.05$), and a higher percentage of patients presenting with serum creatinine greater than 300 μmoles/liter, 22.5% vs. 5.1% ($P < 0.05$). Fourteen biopsies were performed in 11 patients during an episode of macroscopic hematuria (group 1A). One hundred percent of these biopsy specimens showed crescents. Ninety-one percent of 11 biopsy specimens from ten patients (group 1B), taken 3 to 27 days following an episode but at a time when urinary red cells were less than 1,000,000/ml, also showed crescent formation. Of 14 biopsy specimens from 13 patients without macroscopic hematuria, but with greater than 1,000,000 red cells/ml in the urine just prior to biopsy (group 2A), 79% had crescents. In conclusion, macroscopic hematuria in adult patients with mesangial IgA nephropathy is associated with a high likelihood of crescents on renal biopsy specimens and worse renal function. Careful quantitative assessment of the urine for renal bleeding may help to better define the activity of disease in these patients.

Hématurie macroscopique dans la néphropathie mésangiale à IgA: Corrélation avec les croissants glomérulaires et le dysfonctionnement rénal. Cent quatre vingt-six spécimens de la biopsie rénale provenant de 79 malades adultes avec une néphropathie mésangiale à IgA ont été examinées et corrélées aux données cliniques au moment de la biopsie. Quarante malades (groupe 1) avec une histoire d'hématurie macroscopique ont été comparés à 39 malades (groupe 2) sans cette histoire. Les malades du groupe 1 avaient une créatininémie plus élevée, 240 ± 20 μmoles/litre contre 140 ± 10 μmoles/litre ($P < 0,01$), une clearance de la créatinine plus faible, 69 ± 36 ml/min contre 87 ± 30 ml/min ($P < 0,05$), et un plus fort pourcentage de malades ayant une créatininémie plus élevée que 30 μmoles/litre, 22,5% contre 5,1% ($P < 0,05$). Quatorze biopsies ont été effectuées chez 11 malades pendant un épisode d'hématurie macroscopique (groupe 1A). Cent pourcent de ces spécimens de la biopsie montraient des croissants. Quatre-vingt-onze pourcent de 11 spécimens de la biopsie provenant de dix malades (groupe 1B), faites 3 à 27 jours après un épisode, mais à un moment où les hématies urinaires étaient à moins de 1.000.000/ml, montraient également des formations en croissant. De 14 spécimens de la biopsie provenant de 13 malades sans hématurie macroscopique, mais avec plus de 1.000.000 d'hématies/ml dans les urines juste avant la biopsie (groupe 2A), 79% avaient des croissants. Dans conclusion, l'hématurie macroscopique chez des malades adultes ayant une néphropathie mésangiale à IgA est associée à une grande fréquence de croissants à spécimens de la biopsie rénale et à une moins bonne fonction rénale. Une étude quantitative soigneuse des urines à la recherche d'un saignement rénal peut aider à mieux définir l'activité de la maladie chez ces malades.

Mesangial IgA nephropathy is a common clinical pathologic syndrome often accompanied by recurrent episodes of macroscopic hematuria. Since renal function has been thought to be relatively well preserved for prolonged periods, these episodes have been considered to be of little importance [1, 2]. Recently Clarkson et al emphasized the need for prolonged observation of such patients since a gradual decline in renal function was suggested in follow-up studies of 50 patients with characteristic mesangial immunofluorescence for IgA and C3 [3]. These authors and others have found only increased age, proteinuria, and hypertension as variables predicting an overall worse prognosis in this disease [3–6]. This study was designed to correlate clinicopathologic features of patients with mesangial IgA nephropathy and the presence or absence of macroscopic hematuria. The striking association of macroscopic hematuria with focal and segmental proliferation, segmental necrosis and their consequences, namely glomerular crescent formation, are well illustrated. In addition, renal function of patients with macroscopic hematuria at the time of biopsy is worse than similar patients without macroscopic hematuria.

Methods

One hundred and eighty-six renal biopsy specimens from 79 patients with mesangial IgA nephropathy were reviewed. Consecutive patients with this pathologic diagnosis starting backward from June 30, 1981, were used. In all patients the diagnosis was based on the presence of IgA in the glomerular mesangium as the predominant immunoglobulin present. No patient had any evidence of a systemic disease known to be associated with glomerular IgA deposition. Specifically, there was no evidence of systemic lupus erythematosis, Henoch-Schonlein purpura, cirrhosis of the liver, or systemic vasculitis. In patients in whom the first biopsy was done prior to 1970, the diagnosis of mesangial IgA nephropathy became clear only on subsequent biopsies when immunofluorescence was routinely available. For a biopsy specimen to be included in the study, a minimum of ten glomeruli were needed.

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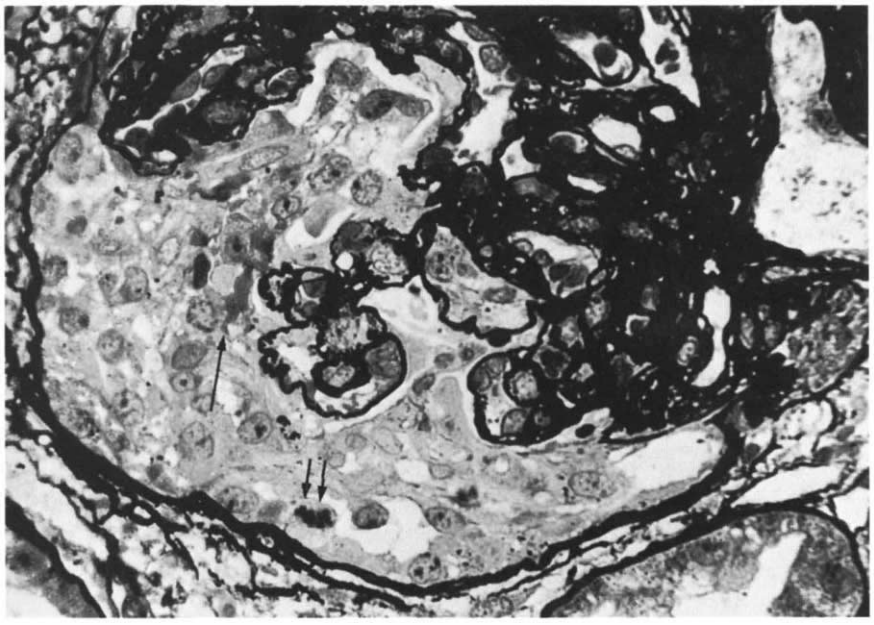

Fig. 1. *Large cellular crescent in a patient with macroscopic hematuria.* Fibrillar fibrin is included in the crescent (*arrow*) which also contains mitoses (*double arrow*). (Silver Masson ×900)

Clinical data were ascertained from the patient's record at the time of each biopsy. This included blood pressure and renal function as measured by serum creatinine and creatinine clearance corrected for body surface area. Values are expressed as micromoles per liter and milliliters per minute, respectively. One milligram per deciliter of serum creatinine equals 88 μmoles/liter. Quantitative estimation of daily urine protein excretion and urinary red blood cell count within the 24 hr preceding the biopsy were also noted. To quantitatively assess hematuria, a 10-ml fresh urine sample was centrifuged for 5 min at ×750*g* in a centrifuge with a swing-out head. From this, 9.5 ml of supernatant was removed, and the resuspended deposit was examined in a Fuchs-Rusenthal chamber, using phase-contrast microscopy (Olympus BH microscope equipped with positive phase-contrast illumination).

In many patients whose biopsies were performed after 1975, serum immunoglobulin A was measured by immunodiffusion. Values greater than 4 mg/ml were considered to be elevated. Circulating immune complexes were determined by modification of the liquid phase Clq binding assay of Zubler and Lambert [7]. Percent binding greater than 4% was considered abnormal. In all 79 patients, serum antistreptolysin 0 titer, C3, C4, antinuclear factor and/or antibodies to DNA were normal or negative. These tests were carried out with commercially available immunodiffusion plates. Urologic causes for bleeding were excluded by intravenous pyelography and cystoscopy in most instances.

Renal biopsy specimens were fixed in Dubosq-Brazil solution, and 24 serial 1-2 sections were cut and stained with hematoxylin and eosin, periodic acid Schiff, Masson's trichrome, Silver-Masson, and Weigerts elastic and counterstained with von Gresoris connective tissue stain. Tissue was snap-frozen and sectioned in cryostat at −20°C and stained by the direct immunofluorescent method with fluorescein-labelled antisera. Commercial antisera against IgG, IgA, IgM, Clq, C3, fibrogen, and albumin were used.

Although tissue samples were taken and preserved for electron microscopy, ultrastructural examination was only performed on 20% of the biopsy specimens to confirm the typical pattern of deposition of immunoglobulin or complexes suggested by light and immunofluorescent microscopy. Biopsy specimens were examined for basic histologic pattern. Any superimposed focal or segmental proliferative hyalinotic and sclerotic lesions as well as the percentage of glomeruli with crescents and total sclerosis were recorded. The type of immunoglobulin or complement deposition in addition to IgA was noted.

The histologic criteria for the designations used in this paper were as follows:

When there was an increase in mesangial matrix and mesangial cells, the designation diffuse mesangial proliferative (DMP) glomerulonephritis was applied. Invariably red staining mesangial deposits were prominent on trichrome stains and electron dense deposits were noted when ultrastructural examinations were performed.

When areas of focal and segmental proliferation were superimposed on the basic pattern, the biopsy specimen was classified as showing focal and segmental proliferative glomerulonephritis (Figs. 1 and 2). In these patients segmental crescents, fibriliar fibrin deposits and necrosis were almost invariable as was evidence of red blood cells in Bowman's space and within tubular lumens (Fig. 3). The final superimposed histologic pattern was focal and segmental hyalinosis and sclerosis (Fig. 4). This pattern was seen in conjunction with focal and segmental proliferative changes or in their absence. The degree of interstitial fibrosis and vascular change was evaluated on a 1-to-3-plus semi-quantitive basis. For purposes of analysis patients were divided into two groups. Patients who had a well documented history of macroscopic hematuria were in group 1 which included a total of 40 patients who underwent 116 biopsies: within group 1 were 14 biopsy specimens from 11 patients in whom biopsies were performed while their urine had macroscopic hematuria and urinary red blood cell counts of

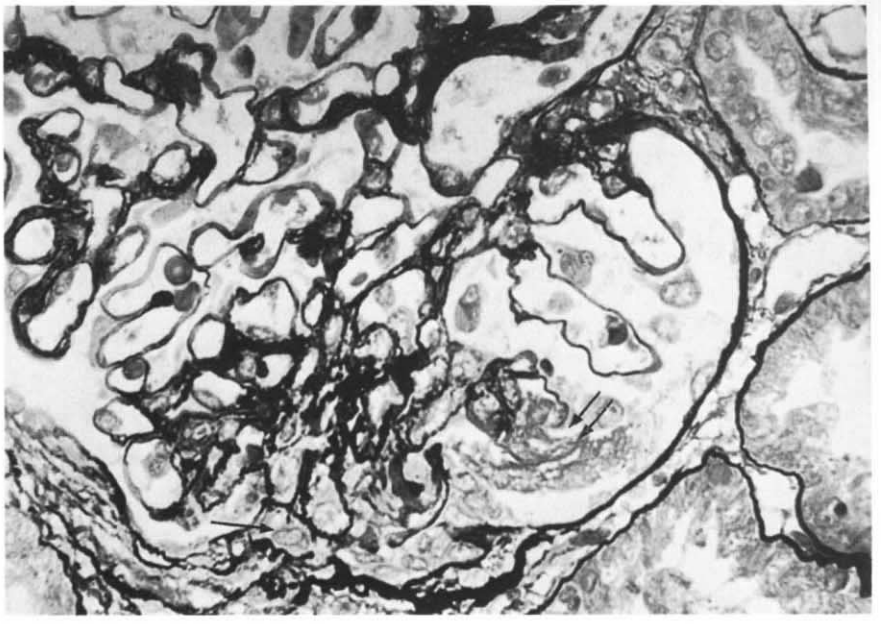

Fig. 2. *Segmental area of sclerosis with healing crescent* (arrow) *in a glomerulus which also shows fibrillar fibrin related to a break in the glomerular capillary wall* (double arrow). (Silver Masson ×900)

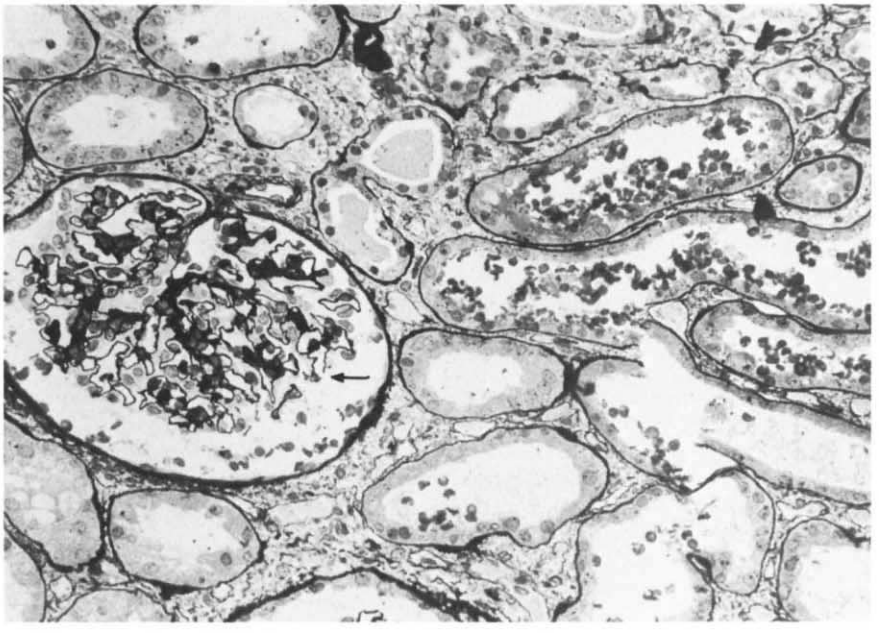

Fig. 3. *Biopsy specimen from a patient at the time of macroscopic hematuria with many red cells in Bowman's space and renal tubules.* The break in continuity of a glomerular capillary (*arrow*) could be the source of this glomerular hemorrhage. (Masson trichrome ×360)

greater than 1,000,000 red blood cells/ml. These 11 patients are considered separately as group 1A. Another subset of 11 biopsy specimens in ten patients, group 1B, were taken within 30 days of an episode of macroscopic hematuria, but at a time when urinary red blood cells were less than 1,000,000 red blood cells/ml and there was no further macroscopic hematuria evident.

Group 2 was comprised of 39 patients who had never had macroscopic hematuria. Seventy biopsies were performed in these patients. Within group 2 there were 13 patients who underwent biopsy at a time when urinary red blood cell counts were found to be greater than 1,000,000/ml, but macroscopic hematuria had not been noted by either the patient or his physician. This subset of 14 biopsy specimens in 13 patients was designated by group 2A.

Groups 1 and 2 were compared in regard to the various clinical and pathologic features by an unpaired t test or χ^2 analysis.

Results

In patients with macroscopic hematuria (group 1) there were 33 males and 7 females who presented at a mean age of 32.9 ± 11.1 years. Group 2 had 25 males and 14 females with a mean age of 37.1 ± 11.7 years. Subgroups 1A, 1B, and 2A had similar ages of 34.6 ± 16, 32.2 ± 11, 36.6 ± 15, respectively. Male to

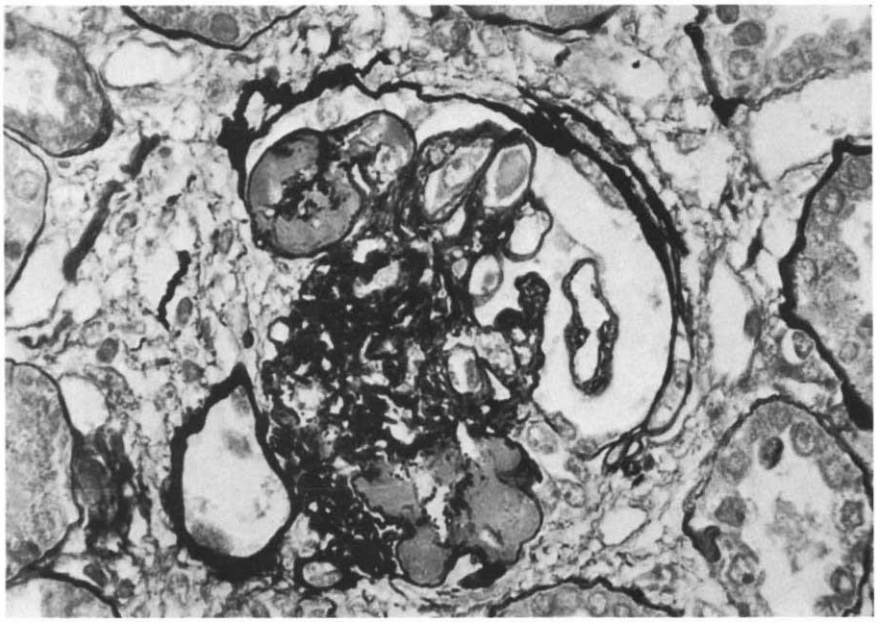

Fig. 4. *Segmental hyalinosis-sclerosis lesion which appears during the healing phase after crescent formation.* (Silver Masson ×900)

female ratios in the subgroups were 8:3, 8:2, and 5:5, respectively. None of the age and sex differences between groups or subgroups reached statistical significance.

Characteristics of patients with macroscopic hematuria (group 1) and without macroscopic hematuria (group 2) are shown in Table 1.

The differences between the groups would be even more striking if patients with microscopic hematuria of greater than 1,000,000 red blood cells/ml of urine (group 2A) were separated from group 2 as a whole. The two patients without macroscopic hematuria who presented with renal failure were both in subgroup 2A. Eleven of the 14 biopsy specimens in the 13 patients in this subgroup had crescents, and 13 of 14 had focal and segmental proliferation. If these patients with heavy microscopic hematuria (greater than 10^6 red blood cells/ml) are compared with the total group of patients without microscopic hematuria, they have initial renal function and heavier proteinuria ($P < 0.05$). Specific data on the three subgroups, groups 1A, 1B, and 2A, with recent macroscopic hematuria and/or greater than 1,000,000 red blood cells/ml are shown in Tables 2, 3, and 4.

Examples of the histologic lesions found in patients with macroscopic hematuria are shown in Figures 1, 2, and 3. A segmental hyalinosis and sclerosis lesion is shown in Figure 4.

There were no statistically significant differences in the extent of proteinuria between any of the groups or subgroups although patients with more severe hematuria tended to have higher daily protein excretion. Likewise, the percentage of patients with hypertension did not differ. In biopsy specimens with crescents the number of glomeruli involved in this process on a percentage basis did not differ among groups or subgroups. However, biopsy specimens from all of the subgroups with macroscopic hematuria or greater than 1,000,000 red blood cells/ml urine at the time of biopsy had a high percentage of patients who had crescentic disease (70 to 100%) as compared to 36.2 and 18.6% in biopsy specimens from groups 1 and 2 as a whole. The percentage of glomeruli that were obsolescent or totally sclerotic did not differ between patients with and without macroscopic hematuria. There were no differences in the semiquantitative scores of vascular and interstitial fibrosis between groups 1 and 2 patients.

The type of immunoglobulin deposition in renal biopsy specimens did not differ between the groups. C3 was present in virtually all biopsy specimens along with IgA in a mesangial distribution. IgM was the next more frequent immunoglobulin, being present in 71% of biopsy specimens followed by fibrin 37%, IgG 16%, and Clq 11%.

Few patients during macroscopic hematuria or at times when red cell counts in the urine were greater than 1,000,000/ml had immune complexes or serum IgA determined. In patients who had these investigations, there were no differences between groups. Twenty-nine percent of the biopsy specimens in patients with a history of macroscopic hematuria in whom immune complexes were measured had positive studies compared to 50% of the biopsy specimens in patients without macroscopic hematuria.

Likewise elevation serum IgA was noted in 31 and 18% of groups 1 and 2 patients, respectively, in whom these studies were done. This difference was not statistically significant.

Discussion

Various histologic patterns have been found on light microscopy in large series of patients with mesangial IgA nephropathy [3–6]. Results of this study suggest that focal and segmental proliferation are associated in a high percentage of patients with macroscopic hematuria and focal crescent formation. When this lesion heals the glomerulus often shows changes of focal and segmental hyalinosis/sclerosis. Patients with similar glomerular immunofluorescence but with only diffuse mesangial proliferation on light microscopy have less hematuria and few, if any, crescents.

It is our understanding that the failure of previous studies to recognize this clinicopathologic correlation may be due in part

Table 1. Comparison of patients with or without history of macroscopic hematuria[a]

	Group 1	Group 2
Number of patients	40	39
Number of biopsies	116	70
Serum creatinine at presentation, *μmoles/liter normal < 110 μmoles/liter*	240 ± 20	140 ± 14[b]
Creatinine clearance at presentation, *ml/min;* normal, *90 to 130 ml/min*	69 ± 36	87 ± 30[c]
Daily protein excretion, *normal < 0.1 g/day*	1.4 ± 1.1	1.0 ± 1.2
% Patients with blood pressure > 150/100	36	28
Serum IgA > 4 mg/ml	12 of 39 biopsies	4 of 22 biopsies
C1 binding > 4%	7 of 24 biopsies	8 of 16 biopsies
% Biopsy specimens with crescents	36.2	18.6[b]
% Biopsy specimens with focal and segmental proliferation	35.9	24.3
% Biopsy specimens with focal and segmental hyalinosis/ sclerosis	35.4	40
% Patients presenting with renal failure *serum creatinine > 300 μmoles/liter* or *< 45 ml/min*	22.5	5.1[c]

[a] Values listed are means ± SD or percentages. The extent of statistical significance is noted by footnotes b and c. When no footnote is present, differences between groups 1 and 2 were not significantly different at $P < 0.05$.

[b] $P < 0.01$.

[c] $P < 0.05$.

[d] Serum creatinine: 1 mg/dl = 88 μmoles/liter.

to the focal nature of the active phase of this disease process. More likely, however, is the proximity of our renal biopsies to the episode of clinical bleeding in groups 1A and 1B patients in our study. Gartner et al [4] found that only 6% of 37 patients presenting with macroscopic hematuria had crescents, however, the precise timing of the biopsy in relation to an episode of hematuria is unclear. Moreover, the method of quantitating urinary red cells used 20 as the number of cells per high power field defining severe hematuria. Previous data have shown that patients with 20 red blood cells per high power field may have between 10,000 and 100,000 red blood cells per milliliter, thus not necessarily displaying the extent of hematuria as in our patients [8]. The patients of Gartner et al also had normal serum creatinine measurements, and only 13 of 153 patients in his total series were biopsied again [4]. Clarkson et al could find no differences in biopsies of patients in exacerbation or remission in regard to macroscopic hematuria [3]. No data were presented concerning the timing of biopsies or the quantification of hematuria in these individuals. Thus, qualitative estimates of hematuria may be misleading, possibly leading to differing interpretations regarding the severity of bleeding and the importance of any associated proteinuria as predictors of a poorer prognosis.

Crescents and proliferation may disappear within a matter of weeks leaving hyalinotic and sclerotic lesions as their only residua [9]. Thus, patients who had biopsies more than 30 days following an episode of macroscopic hematuria had a much lower prevalence of crescents and proliferative lesions and higher prevalence of hyalinosis and sclerosis.

It should be noted that patients without macroscopic hematuria on whom biopsies were performed when urinary red cells were greater than 1,000,000/ml show similar morphologic changes to patients with macroscopic hematuria. If these patients had been excluded from an analysis of the total group of patients without macroscopic hematuria, differences between groups 1 and 2 obviously would be even more striking. Previous reports concerning the importance of macroscopic hematuria may have excluded patients who quantitatively had large numbers of urinary red cells by relying only on history. Examination of the urinary sediment quantitatively is both cheap and simple. The presence of more than 1,000,000 red cells/ml urine strongly suggests that the underlying glomerular disease is active and that crescentic change is likely. In addition, by examining the sediment with phase contrast microscopy, confirmation of the glomerular origin of the hematuria may be obtained [10, 11].

Follow-up studies of patients with mesangial IgA nephropathy are relatively short-term [3, 5, 6] or contain small numbers of patients [1, 2, 4, 12]. In the report of Hood et al, five of 37 patients developed renal failure over a mean follow-up of less than 3 years [5]. Although few patients had segmental necrosis or crescents on the initial biopsy, 78% of these patients experienced single or repeated episodes of macroscopic hematuria. The timing of renal biopsies to episodes of macroscopic hematuria was not stated. Berger, who initially described mesangial IgA nephropathy in 1969 [13], recently revised his earlier optimistic view of prognosis concluding that as many as one third of mesangial IgA patients will ultimately develop renal insufficiency [14]. The numbers of patients with crescentic change on initial biopsy or at times of macroscopic hematuria is unknown.

If crescents accompany various morphologic types of glomerulonephritis, the prognosis is thought to be worse [15, 16]. If more than 80% of glomeruli are involved by crescents, progression to renal failure usually proceeds rapidly. It is possible that development of renal failure depends on the extent, frequency, and severity of cycles of segmental proliferation, necrosis and crescent formation. The patients with IgA nephropathy and episodes of macrohematuria have the potential for this type of course based on biopsy findings at the time of heavy bleeding.

The pathogenesis of mesangial IgA nephropathy and its subsequent progression of renal failure is unknown [17]. Although elevated serum IgA levels theoretically might play some role as was suggested by Hood et al [5], a controlled trial of phenytoin which lowered serum IgA levels to normal failed to affect disease progression [18]. Moreover, our study and others show that only 30 to 50% of patients have elevated circulating IgA concentrations [3, 16].

Table 2. Patients (subgroup 1A) with mesangial IgA nephropathy biopsied during an episode of macroscopic hematuria[a]

Patient no.	Age/Sex	Histologic pattern	Crescents %	Glomeruli sclerosed %	Serum creatinine *μmoles/liter*	Creatinine clearance *ml/min*	Blood pressure *mm Hg*	24-hr Protein excretion *grams*
1	39 F	DMP; FSP; FSH-Sc	27	18	140	47	132/70	4.3
2	56 F	DMP; FSP	17	33	210	40	155/105	2.4
3	17 M	DMP; FSP	5	18	80	126	160/100	0.8
		DMP; FSP	6	20	70	126	136/80	1.1
4	15 M	DMP; FSP	12	0	90	108	125/75	1.2
5	61 M	DMP; FSP	6	45	820	9	135/95	0.4
		DMP; FSH-Sc	10	43	900	6	140/100	0.1
6	27 M	DMP; FSP	20	10	90	144	128/82	1.7
7	50 M	DMP; FSP	40	0	700	.4	160/90	1.2
8	37 M	DMP; FSP	13	25	110	90	180/110	2.0
9	19 M	DMP; FSP	12	10	350	24	130/85	1.5
10	37 M	DMP; FSH-Sc	11	11	350	27	175/112	0.7
11	22 F	DMP; FSP	33	0	105	60	160/110	2.5
Total mean ± SD			*18 ± 13*	*16 ± 14*	*290 ± 20*	*72 ± 66*		*1.7 ± 1.1*

Abbreviations: DMP, diffuse mesangial proliferation; FSP, focal and segmental proliferation; FSH-Sc, focal and segmental hyalinosis/sclerosis.
[a] One hundred percent of the biopsy specimens had focal and segmental crescent formation. Two patients presented with severe renal failure.

Table 3. Patients (subgroup 1B) with mesangial IgA nephropathy who had biopsies within 3 to 27 days of macrohematuria[a]

Patient no.	Age/Sex	Histologic pattern	Crescents %	Glomeruli sclerosed %	Serum creatinine *μmoles/liter*	Creatinine clearance *ml/min*	Blood pressure *mm Hg*	24-hour Protein excretion *grams*
12	45 M	DMP; FSP	20	0	110	88	128/80	0.8
13	30 M	DMP; FSP	5	40	90	72	155/105	1.2
14	19 M	DMP; FSP	0	0	80	66	110/60	0.1
15	35 M	DMP	8	33	90	72	165/115	3.4
16	31 F	DMP; FSP	8	17	80	60	125/85	0.2
17	18 M	Diffuse endocapillary proliferation	11	0	100	22	150/100	0.7
18	29 M	DMP; FSP; FSH-Sc	4	83	320	30	168/108	0.2
19	33 M	DMP; FSP	13	13	100	138	170/100	1.9
		DMP; FSP; FSH-Sc	13	18	110	120	140/95	1.5
20	17 M	DMP; FSP	9	0	600	24	115/65	1.2
21	42 F	DMP; FSP	100	10	900	6	185/125	0.1
Total mean ± SD			*17 ± 28*	*14.5 ± 25*	*230 ± 270*	*58 ± 42*		*1.2 ± 1.0*

Abbreviations: DMP, diffuse mesangial proliferation; FSP, focal and segmental proliferation; FSH-Sc, focal and segmental hyalinosis/sclerosis.
[a] Less than 10^6 red cells are present per milliliter of urine. Ninety-one percent of the biopsy specimens had focal and segmental crescent formation. Two patients presented with severe renal failure.

Circulating or in situ immune complex formation is more likely to play a role in initiating and maintaining tissue injury. Woodroffe et al were able to find circulating immune complexes in 64% of episodes of macroscopic hematuria [19]. We have too few data during acute episodes to corroborate this, however, it is clear that positive tests may occur in such patients at times when hematuria is not excessive. Variations in the pathogenesis and course of the mesangial IgA syndrome from various centers could be due to different types of complexes formed by certain individuals in response to disparate infectious or environmental antigens. It is interesting to note the relatively high percentage of biopsy specimens containing IgG in Europe and North America [4, 5, 13, 20] in contrast to the Australian biopsy specimens in which IgM is the most common immunoglobulin found accompanying C3 and IgA [3, 19].

Based on the clinical and histologic observations in this study, we would suggest that focal breaks in the glomerular basement membrane as a result of segmental proliferation lead to crescent formation. Consistent with this formulation are the observations of Kupor, Mullins, and McPhaul [21], Shigematsu et al [22], and Sakai, Kitajima, and Kawamura [23] who reported segmental tuft adhesions and crescents in from 17 to 30% of the biopsy specimens in patients with idiopathic renal hematuria and IgA nephropathy. Shigematsu et al [22] demon-

Table 4. Patients (subgroup 2A) without macroscopic hematuria but with $>10^6$ red cells/ml urine[a]

Patient no.	Age/Sex	Histologic pattern	Crescents %	Glomeruli sclerosed %	Serum creatinine *μmoles/liter*	Creatinine clearance *ml/min*	Blood pressure *mm Hg*	24-hour Protein excretion *grams*
22	36 M	DMP; FSP	8	42	170	57	185/115	0.5
23	23 F	DMP; FSH-Sc	0	0	80	84	122/78	3.8
24	49 M	DMP; FSP	11	33	190	45	135/85	0.2
25	28 F	DMP; FSP	25	58	160	52	65/115	3.4
26	29 F	DMP	0	40	50	174	105/70	0.4
27	28 M	DMP; FSP	7	13	160	90	140/90	0.3
28	44 M	DMP; FSH-Sc	15	10	80	104	128/84	0.8
29	25 F	DMP; FSH-Sc	44	8	80	54	136/88	1.2
30	45 M	DMP; FSP; FSH-Sc	50	23	700	6	165/110	4.0
31	48 M	DMP; FSP; FSH-Sc	0	45	190	42	130/85	3.5
32	18 M	DMP; FSP	5	10	60	120	150/105	1.5
33	64 M	DMP; FSP FSH-Sc	100	50	800	6	165/105	0.6
34	37 F	DMP; FSP	15	40	100	66	125/75	4.0
		DMP; FSP	52	44	280	36	130/85	2.0
Total mean ± SD			*25 ± 32*	*31 ± 20*	*340 ± 50*	*64 ± 48*		*1.9 ± 1.6*

Abbreviations are as in Table 3.

[a] Seventy-nine percent of the biopsy specimens had crescent formation. Two patients presented with renal failure severe enough to require dialysis.

strated that focal breaks in the glomerular basement membrane with fibrin and red cells demonstrable in Bowman's space are associated with focal and segmental proliferative lesions and crescents in IgA nephropathy. Similar changes have been noted in association with crescents in other glomerulopathies [24, 25]. The pathophysiologic mechanism resulting in reversible declines in glomerular filtration rate is less clear. Recent data suggest that glomerular bleeding per se may result in morphologic evidence of tubular injury and intratubular obstruction [26].

Thus, mesangial IgA nephropathy associated with recent macroscopic hematuria and/or more than 1,000,000 red blood cells/ml urine carries a high likelihood of focal and segmental proliferative changes with crescents on renal biopsy specimens. In patients without recent macroscopic hematuria and less than 1,000,000 red cells/ml, the presence of focal and segmental sclerosis and hyalinosis most likely represents a healing stage of a prior proliferative lesion. Episodes of macroscopic hematuria are often associated with renal dysfunction which are frequently reversible. In management of patients with mesangial IgA nephropathy quantitative assessment of renal bleeding may provide useful information.

Acknowledgments

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